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April 24, 2002

Mr. Joe Levitt, Director
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: GRAS Notice No. GRN 000091; Food Additive Petition FAP 6A3930

Dear Mr. Levitt:

On February 28, CSPI filed a complaint with the FDA about Marlow Foods Ltd.'s Quorn-brand foods and their mycoprotein ingredient. We would like to provide some additional information. We trust that the FDA will consider this information prior to making final decisions on the food additive petition for mycoprotein.

I. Labeling

We complained that labels compare mycoprotein to mushrooms. We asked mycologists for their opinion of that comparison. What they said supports our allegation that Quorn products are deceptively labeled:

- Three mycology experts at Pennsylvania State University have written: "While it is true that *F. venenatum* [the fungal strain used in Quorn products] and mushrooms are both fungi, calling *F. venenatum* a mushroom is analogous to calling a rat a chicken because both are animals."¹
- Kathie Hodge, assistant professor of mycology at Cornell University, says *Fusarium*'s taxonomic relationship to mushrooms is analogous to humans' relationship to jellyfish.²

The label claim "made from natural ingredients" that appears on all Quorn products is misleading because Quorn's mycoprotein is not minimally processed.³ At one point in the

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¹ Geiser DM, Kulda GA, Baroni TJ. Letter to Joe Levitt, FDA/CFSAN, March 5, 2002.

² Pers. Comm., March 1, 2002.

³ This modifies our earlier letter, which accepted the naturalness of Quorn's mycoprotein.

manufacturing process the ingredient is treated in such a way as to reduce its content of RNA:

Since the purine bases in nucleic acids are metabolized to uric acid, foodstuffs should be treated, if possible, to reduce their RNA content to minimize any increases in serum uric acid. Therefore in the production of mycoprotein, its RNA content is reduced from 10% to less than 2% (dry weight) by rapidly heating the fermenter "broth," a process which causes complete loss of viability and loss of most of the cell RNA into the supernatant. Following RNA reduction, the suspension is recovered by a centrifugation dewatering process in the form of paste.⁴

According to a news account, Deputy FDA Commissioner Lester Crawford told a congressional subcommittee on March 21: "If it's on the label, it has to be true, and it's up to us to be sure that it is." We agree. The Quorn labels are a perfect place to convert those thoughts into action.

II. Safety

The company's June 1999 GRAS-panel report (and submission to the FDA) cursorily explains away concerns about allergenicity. It states (page 16):

(iv) Human Clinical Studies: Four studies were conducted to assess acceptability of myco-protein as a food and any intolerance. The results indicated that myco-protein is well tolerated in human trials with an extremely low allergenic potential. The Expert Panel concluded that mycoprotein is well tolerated in humans.

That report did not give literature citations for the studies or provide any further discussion. The GRAS notification (submitted by Stuart M. Pape for Marlow Foods) provided a sentence or two more discussion of the four studies, but provided no basis for concluding that mycoprotein is safe. It cited two published studies to support the statement "A significant history of use in Europe has also demonstrated that humans tolerate mycoprotein well, and human use has been examined in published studies." However, it also acknowledged that an unspecified number of human volunteers who were "atopic to fungus-derived foods" *did* experience recurring adverse reactions in studies.⁵

The first study, by Tee et al, examined ten people who had complained that they vomited

⁴ Rodger G. Production and Properties of Mycoprotein as a Meat Alternative. Food Technology; July 2001. Rodger is research and development manager for Marlow Foods. <http://www.ift.org/developingfoods/production.html> (accessed 4/7/02)

⁵ Marlow Foods. GRAS notification for Mycoprotein. Submitted by Marlow Foods, Nov. 30, 2001, p. 23.

and had diarrhea after eating Quorn products.⁶ Tee, et al., found that two complainants reacted to a skin-prick test using freeze-dried (but not "fresh") Quorn mycoprotein or product, and several other mold-sensitive subjects (non-complainants) had RAST responses. The researchers concluded:

The adverse symptoms reported after ingestion of Quorn were remarkably consistent in their nature and timing.... Specific IgE antibody to mycoprotein was not significantly raised in any complainant. The possibility can not be excluded of participation of fungal polysaccharide allergens, which RAST testing would probably not detect, or of non-IgE associated mechanisms. Intolerance to ingested Quorn reported by a small number of consumers may be due mainly to an idiosyncratic response.

The "largely negative results are important and reassuring," concluded the researchers, but CSPI finds it highly disconcerting that a novel, unnecessary new product might cause such "remarkably consistent" "idiosyncratic" gastrointestinal symptoms. Reinforcing our concern is the fact that CSPI has begun receiving reports of vomiting and diarrhea, as discussed by Tee et al., from people who ate Quorn products in the United Kingdom or U.S.:

- A 22-year-old male professional in Massachusetts ate one-third of a package of Quorn Chicken Style Recipe Tenders. About three to four hours later his stomach started getting queasy and he began feeling gassy and felt a need to burp repeatedly. Thirty minutes later he vomited most of his dinner. Over the next two hours he vomited three or four more times until his stomach was essentially empty and experienced mucus production and a swollen and pale face. He was not able to work the next day. Since he thought that he had the flu, he hadn't considered that the Quorn might have caused his problems. Eight days later he ate about 15 Quorn Chicken Style Nuggets. Four hours after eating the product, he felt queasy, and then he vomited within 30 minutes and again later that night. He has no known allergies.
- A 35-year-old businesswoman in Maryland ate two servings of Quorn Tenders. Four hours later she started to feel digestive symptoms, and several hours later she experienced severe vomiting intermittently for four to five hours. She also had watery diarrhea and got dehydrated. She is sensitive to wheat and tries to avoid it (the Quorn product does not list wheat as an ingredient).
- A 35-year-old professional woman in Edinburgh, Scotland, ate Quorn products on three different occasions and each time, about three hours later, experienced severe vomiting and diarrhea. After the third occasion she realized that Quorn was the only consistent thing she had eaten each time she was sick. She ate it a fourth time by mistake, when

⁶ Tee RD, Gordon DJ, Welch JA, Newman Taylor AJ. Investigation of possible adverse allergic reactions to mycoprotein ("Quorn"). *Clinical and Experimental Allergy* 1992; 23:257-60.

somebody served it to her unaware that it made her ill. She was violently sick, possibly the most sick she had ever been, and when she checked the label she discovered the product contained Quorn. She has no allergies, except possibly to *Candida albicans*.

- A 26-year-old student in The Netherlands initially had no problem eating Quorn products. However, after the products were labeled "improved" several years ago, several times she experienced nausea and vomiting about two to three hours after eating Quorn "stukjes en des" (Dutch label). She recently "retested" herself and had the same reaction. She apparently still can tolerate small amounts of the product (under 100 g). As a child, she had allergies to milk, shellfish, and large quantities of iodine.
- A 51-year-old Virginia scientist ate Quorn Fillets Provencale while in London. Ten minutes later, his upper lip became numb and somewhat swollen, as did his left cheek. He self-medicated with benadryl. He has no known food allergies.

Neither Tee, et al., nor apparently any other researchers have conducted food challenges in people who believe they are sensitive to mycoprotein. The FDA should ensure that such studies are conducted both to verify that Quorn is causing illnesses and, if it is, to identify the exact component that is causing the problem.

In the second study, Udall, et al., fed subjects one of two different species of fungus. Though one fungus, *Fusarium graminearum*, is in the *Fusarium* genus, it is not the same species as is used to produce Quorn's mycoprotein so it is unclear whether the study has any relevance whatsoever. The second fungus was *Paecilomyces variotii*. The researchers stated: "Mild rashes possibly related to one of the microfungus food products occurred in two [out of 50] individuals fed *P. variotii*." Again, the relevance of that observation is questionable, because the fungus is unrelated to *F. venenatum*.


Thus, the paucity of research on the potential allergenicity of Quorn mycoprotein, with one study indicating possible problems, coupled with reports of adverse reactions in consumers should have precluded the agency from stating that "it has no questions at this time" in response to Marlow Foods' GRAS notification. The FDA's streamlined procedures for responding to GRAS notifications within 90 days (proposed Sec. 170.36(c)(4)(i)(B)) "requires that the notice summary of a scientific procedures GRAS determination include a comprehensive discussion of any reports of investigations or other information (e.g., adverse event reports and consumer complaints) that may appear to be inconsistent with the GRAS determination."⁷ Marlow Foods failed to provide such a discussion of the adverse reactions that it had received and that were one

⁷ U.S. Department of Health and Human Services, Food and Drug Administration. Substances Generally Recognized As Safe, Proposed Rule. Fed. Reg. Vol. 62 (April 17, 1997), 18937-18964.


of the subjects of Tee, et al.'s, research.⁸

The information we have provided should impel the agency to rescind its "no questions at this time" response and begin asking Marlow Foods many questions about its product. The same information certainly should preclude the FDA from approving this mycoprotein as a food additive. The FDA, among other things, should evaluate all the adverse-reaction reports that Marlow Foods and others have received. Also, the FDA should require the company to conduct food challenges with individuals who believe they are sensitive to mycoprotein *before* FDA finalizes its decision on food-additive status of the product. More broadly, *before* approving this mycoprotein, not after, the FDA should establish testing standards for assessing the potential allergenicity of new proteins that companies want to introduce into the American diet. Considering the plethora of tasty, nutritious meat alternatives on supermarket shelves, there is absolutely no need for Marlow Foods' product, no need for the FDA to accept it as GRAS, and no need to approve it as a food additive without ensuring a "reasonable certainty of no harm." Such assurance currently is lacking.

Thank you for your attention to this matter.


Michael F. Jacobson, Ph.D.
Executive Director

Sincerely,


Doug Gurian-Sherman, Ph.D.
Scientific Director, Project on Biotechnology

cc: Lester Crawford, Alan Rulis, Christine Taylor, Bradford Williams

⁸ Ibid., p. 18941-2. The shallowness of FDA's review under its streamlined review process for GRAS notifications undermines the agency's belief "that the substitution of the proposed notification procedure for the current GRAS petition process would not adversely affect the public health..." and throws into doubt whether "replacing one voluntary administrative process with a different voluntary administrative procedure" would, indeed, be "neutral."

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1875 Connecticut Avenue, N.W., Suite 300
Washington, D.C. 20009-5728

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

